Renal vascular changes produced by the mercurial diuretic salyrgan.

By

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With 3 Figures in the Text.

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It is generally stated that mercurial diuretics do not change the hemodynamics of the kidney. On the other hand, reductions in kidney volume, renal blood flow and glomerular filtration have been described by a number of independent investigators, while DICKER has shown that in rats salyrgan increases the diodrast and inulin clearances. A study of the available literature indicates that mercurials can produce several qualitatively and quantitatively different effects on the renal hemodynamics. In the present study an attempt will be made to characterize these mercurial-induced renal vascular changes in the dog and to elucidate the importance of these changes in the response of the kidney to these diuretics.

Methods: The mercurial employed was salyrganic acid (2-[(2-hydroxymercuri-3-methoxy-propyl) carbamyl] phenoxyacetic acid) which was dissolved in an equivalent amount of sodium hydroxide. Anaesthetized dogs weighing 8 to 17 kgms. were used in the present experiments. Pentobarbital anesthesia was induced with 30 mgm. per kgm. given intravenously followed by a continuous infusion of 0.03 to 0.06 mgm. of pentobarbital per kgm. per minute. The animals received either isotonic (0.86 per cent), hypertonic (2 per cent), or hypotonic (0.2 per cent in 3 per cent glucose) sodium chloride infusions into the external jugular or femoral vein. For purposes of renal clearance determinations the saline infusions contained adequate amounts of creatinine or inulin and para-aminohippurate. The clearance rate of para-aminohippurate, at low plasma concentrations (0.5—2 mg. per cent) was considered to be the effective renal plasma flow while glomerular filtration was measured by the renal clearance of inulin or creatinine. Details of the theoretical and practical considerations for these determinations have been discussed by Smith and Goldberg and Chasis. Creatinine was determined by the method of Folin and Wu while inulin was measured by Schreiner's method. Para-aminohippurate was determined in plasma and urine by the method of Smith, et al. Sodium and potassium in plasma and urine were determined by means of

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an internal standard flame photometer. Clearance determinations were usually begun about 60 minutes after the priming injections and constant infusion had been started. All blood samples were obtained from the femoral artery by means of an inlying arterial needle and heparin was the anticoagulant used in all the blood samples. Blood pressure was continuously recorded by means of a mercury manometer attached to the common carotid artery. Urine was collected by means of an inlying bladder catheter or by cannulating the individual ureters. The latter procedure made it possible to determine renal clearances on individual kidneys.

Direct renal blood flow was determined with a bubble flow meter interposed between the left common carotid and left renal artery. The anticoagulant used was heparin and 5 mg. per kgm. was given initially followed by a constant infusion of approximately 0.5 mg. to 1 mgm. per kgm. per hour. The largest possible cannulae were introduced into the vessels and in most instances renal blood flow was interrupted for less than two minutes for introducing the cannula into the renal artery. The bubble flow meter was standardized after each experiment and details concerning the use and limitations of this apparatus have been described.

In the present studies the assumption is made that glomerular filtrate is an ultrafiltrate of plasma. The evidence available indicates that urinary sodium excretion is determined by the relation of sodium filtered in the glomeruli and the amounts of sodium reabsorbed by the renal tubules.

The following abbreviations will be used:

- GFR = glomerular filtration rate determined either by inulin or creatinine clearance.
- PNa = Plasma sodium concentration (mM/l).
- GFRNa = Sodium filtration rate.
- UNa = Urinary sodium concentration (mM/l).
- V = Urine volume (cc per min).
- UNa X V = Sodium excretion (mM per min).
- GFRNa- (UNa X V) = Sodium reabsorbed by the tubules.
- RPF = Renal plasma flow determined by the paraaminohippurate (PAH) clearance at low plasma concentrations.

All values have been calculated on the basis of one m² of body surface. Surface area was calculated by the formula:

\[ Wt. \text{kgm.} \times 0.107 = M. \]

Results: The action of salyrgan on renal blood flow: Möller has shown that salyrgan reduces the kidney volume and that this decrease usually precedes the diuresis. Farah and Maresh have confirmed this observation and have described an acute depression of renal blood flow in dogs. Duggan and Pitts have described a depression of the renal circulation produced by the mercurial diuretic mercuhydrin, which could be prevented by infusions of isotonic sodium chloride. Differences in the mechanisms of production of these effects were probable and thus a restudy of these phenomena was indicated.

Three distinct types of depressions of renal blood flow could be characterized. The first or early type of depression of renal blood flow was studied by direct renal blood flow determinations by means of a bubble